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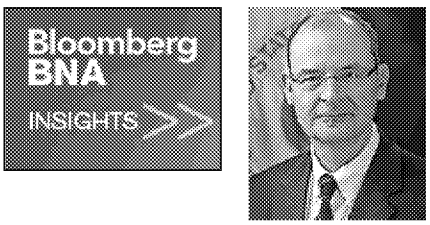
Epidemiology
Risk Assessment

The study of how disease moves through populations is a staple of public health practice. Epidemiology is playing an increasingly important role in environmental health decisions on air, pesticides, water and waste.

Epidemiology: A Foundation of Environmental Decision-Making



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In August 1854, a cholera epidemic swept through London's Soho neighborhood, leaving more than 500 dead in just 10 days. London physician John Snow mapped the cases and realized that those who had contracted cholera had consumed water from the Broad Street pump. On September 7, 1854, Snow took his data to city officials and convinced them to remove the handle of the pump, effectively ending the epidemic. This event–and John Snow's scientific observation–is considered by many to be the beginning of modern epidemiology.

According to the Centers for Disease Control and Prevention, epidemiology is "the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems." It can provide information critical to controlling disease and improving the health of a population, and thus, it is a cornerstone of public health.

At EPA, many of our decisions start with risk assessment, and epidemiology can play a critical role in this process. Human health risk assessment begins by identifying a chemical's hazards and evaluating the relationship between the dose of a chemical and the health effect (dose-response assessment). Epidemiology can provide valuable information as we evaluate whether a pollutant causes a health hazard. Epidemiology can also inform our understanding of the pollutant's dose-response relationship. Understanding how real-world exposures are related to changes in people's health has been the foundation for many of EPA's decisions to protect public health.

Epidemiology studies are considered the gold standard for risk assessment and public health decision-making. They are valued over other types of information—such as traditional animal toxicology studies—for several reasons. First, they are conducted in the species of interest—the human—so we do not have to address the challenge of extrapolating from one species to another. Second, they provide information on human variability and susceptibility that can never be accomplished using animal or human clinical studies. Finally, epidemiology studies of environmental exposures examine more realistic durations of exposure (i.e., longer than those observed in experimental studies) and health effects that generally occur at lower—and more human-relevant—levels of exposure. Because of these advantages, EPA's risk assessment guidelines are clear that human data are generally preferable over animal data and should be given greater weight in hazard characterization and dose-response assessment (48 DEN B-1, 3/11/16).

In assessing causality, epidemiology studies play a critical role. A body of epidemiological literature—alone or in combination with experimental studies—can provide evidence of a relationship between environmental exposures and health effects. Epidemiology can directly inform potential risk reduction strategies, and is relied upon at EPA—and around the world—to inform risk assessment and public health decision-making. In fact, much of EPA's success over the past 45 years has been the result of epidemiology informing our understanding of environmental exposures and risk.

For example, epidemiology has played a central role in the dramatic improvements in air quality that have occurred since the inception of the Clean Air Act. As early as 1948, with the Donora, Pa., smog incident, there were clear indications of a relationship between poor air quality and health effects. However, it was not until the London fog episode of 1952 that it became evident through epidemiology that there was an association between air quality and health. In the years that followed, epidemiology formed the basis of the initial work demonstrating an association between ambient exposures to particulate matter (PM) and health, specifically mortality. The research community—in a quest to better understand the biological mechanisms by which PM exposure causes health effects—began to conduct animal toxicology and human clinical studies. This extensive effort and the resulting body of work ultimately led to the surprising finding that PM can impart effects on the cardiovascular system. Without the initial epidemiology studies reporting an association with mortality, the subsequent experimental studies—which demonstrated that something that enters the body through the lungs can have cardiovascular effects—would never have been conducted. It was through the combination of epidemiologic and experimental evidence that the link between PM exposures and health effects was strengthened. Although the experimental evidence has been instrumental in understanding the relationship between PM exposure and health, it is the extensive epidemiologic evidence that is able to demonstrate health effects across diverse geographic areas and populations at ambient concentrations. And it is ultimately the epidemiology database that has been crucial in setting the level of the National Ambient Air Quality Standard (NAAQS) for PM.

Another example is lead. Since the time of the ancient Romans in the first century BC, people have recognized the health impacts of lead by observing effects in individuals. By the 1800s, there were written clinical descriptions of lead poisoning. By the turn of the century, the U.S. was both the leading producer and consumer of refined lead, which was used as an anti-knock agent in gasoline beginning in the 1920s. New methods for measuring lead in biological media were developed in the 1960s and several studies began to incorporate these biological exposure metrics in analyses examining the relationship between blood lead levels and health effects. By the 1970s, there was clear evidence that lead from gasoline emissions posed a significant public health hazard. EPA recognized at the time that young children were sensitive to lead-related health effects and based the 1978 ambient air quality standard on preventing most U.S. children from exceeding blood lead concentrations that were associated with impaired heme synthesis. The ambient air quality standard for lead was revised in 2008 in consideration of new epidemiology studies linking much lower blood lead concentrations to cognitive effects, such as IQ decrements, in children. Neurodevelopmental and other effects continue to be observed in epidemiologic studies of populations with lower and lower mean blood lead levels and no exposure threshold for these effects is evident. EPA continues to take action to control environmental sources based on this large body of epidemiology and the clear implications for public health.

As science advances, epidemiology data will continue to play a key role in the agency's understanding of the connections between environmental exposures and health effects. For example, refinements in exposure measures have greatly enhanced the ability of epidemiology studies to identify relationships between contaminant exposure and disease outcomes. In early epidemiology studies, exposures may have been estimated based on where people lived or work. As the field advanced, exposure measures became more specific. For example, a study might have differentiated who in an industrial plant actually worked with a particular chemical. Moving forward to today, many epidemiology studies are based on individual-level exposure profiles which have vastly improved our ability to understand the exposure-response relationship. Moreover, mapping of contaminant concentrations using geospatial models and other tools has resulted in similar advancements in environmental epidemiology. As exposure measures become more sophisticated in the future, we will likely be able to increasingly rely on epidemiology data for quantitative risk assessment.

More sophisticated modeling tools will improve our ability to use epidemiology data in risk assessment. Coupling physiologically based pharmacokinetic modeling with human biomonitoring data yields a powerful tool to understand internal dose. And as sensor technology becomes more sophisticated and less expensive, phone "apps" may enable epidemiologists to access individual-level data that we couldn't have imagined two decades ago.

As our understanding of clinical disease progresses, we will have information about subclinical markers or predictors of disease—such as coronary calcium content as a predictor of atherosclerosis or chromosomal aberrations and micronuclei as predictors of cancer risk—that will help us connect the dots in ways we previously were not able to. Associating environmental exposures with these types of biomarkers, which occur more often and become discernable more quickly, allows more powerful analyses of rare diseases. As we learn more about genetic variability, epidemiology will prove invaluable to further our understanding of those populations at greatest risk of a health effect due to an environmental exposure and how environmental exposures interact with genetics to influence health and disease.

These are some compelling reasons to use epidemiology data to inform our understanding of risk. However, there are also challenges. The following articulates some of these challenges and offer recommendations to address them:

1. Discordant Results: In some cases, there is an epidemiology study that shows effects at a low level of exposure, but we have animal toxicology data that do not show these same effects at a higher exposure level. In this situation, some may say that the epidemiology is flawed (e.g., from confounding factors) and the results are biased. However, the full body of scientific literature needs to be evaluated appropriately by scientists with the relevant skills and expertise. We must examine each study—and the entire database of information as a whole—to determine if there are attributes of the epidemiology data that might lead to a false positive or spurious results. Likewise, we must determine if there are attributes of the animal data that would lead to a false negative or a

failure to identify the relevant hazard. It is also important to remember that even though a study may be imperfect, it can make an important contribution to the understanding of the entire collective body of evidence.

2. Appropriate Expertise: At an agency like EPA, we have many scientists with toxicology expertise, but we have fewer scientists with epidemiology expertise. As the use of epidemiology in risk assessment and decision-making becomes more common—and as the field advances so we have a strengthened understanding of exposure and disease processes—we need to ensure we have the relevant expertise to evaluate the strengths and limitations of epidemiology studies in terms of how they inform our understanding of risk. We will need to make sure that our scientists remain current in the field and are trained appropriately as the field of epidemiology advances. Equally as important will be ensuring we have appropriate expertise on agency peer review panels. Well-trained experts in epidemiology will be critical to providing a robust peer review as we more frequently rely on epidemiology in risk assessment.

3. Systematic Review and Risk Assessment: As EPA increasingly uses systematic review approaches to evaluate the literature when developing a risk assessment (31 DEN A-2, 2/17/16), those researchers conducting epidemiology studies should be aware of the elements that are needed to allow EPA to make full use of the available data. For example, presenting more details of the environmental data used in a study (means and distributions) increases confidence in risk estimation.

4. Confidentiality: Although providing transparency to the public is critical, it must be balanced against EPA's equally important responsibility to maintain confidentiality and protect individual privacy. A range of personal data is collected in many epidemiology studies, and without maintaining confidentiality we jeopardize our ability to conduct future studies that ultimately could inform decision-making and protect public health.

5. Study replication: There has recently been increased interest in demonstrating study replicability, but it is important to understand that epidemiology studies are different from traditional animal toxicology studies in that they can never be exactly replicated (e.g., with the same people, in the same place, with the exact same exposures, and over the same period of time). This lack of a laboratory-type replicability, however, does not weaken an epidemiology study's findings. As replication of many epidemiologic studies is impractical, epidemiology relies upon careful causal evaluations based on the available literature to assess the specific strengths and weaknesses of each study and the consistency of the evidence with regards to chance, confounding, and other biases. Likewise, having studies that examine associations in different populations and exposure settings increases the strength of causal conclusions.

Epidemiology can provide powerful scientific evidence for EPA as we examine the hazards of an environmental exposure, develop risk estimates, and make decisions designed to reduce or eliminate harmful exposures and protect public health. The field has advanced tremendously since John Snow and the Broad Street Pump. However, just as Snow's removal of the pump handle stopped an epidemic in its tracks, 21st century epidemiology can inform public health decisions that are equally powerful. So the bottom line is this—EPA is a public health agency, and epidemiology has been and will continue to be the cornerstone of public health.